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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,572	06/18/2001	Reto Naef	4-30754A	2901

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 04/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/883,572	Applicant(s) NAEF, RETO	
	Examiner Mina Haghighatian	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21 and 25-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21, 25-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 21, 26-27 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9428902 in view of Sui et al (6,077,841).

WO 9428902 teaches a pyrazolopyrimidinones for treatment of impotence (page 1, lines 1-8). Especially preferred individual compounds for such treatment include 5-[2-rthoxy-5-(4-methyl-1-piperazinylsulphonyl)-phenyl]-1-methyl-3-n-porpyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (pages 6-7 & 11). WO 9428902 lacks disclosure on specific routes of administration.

Sui teaches substituted 5-heterocyclyl pyrazolopyrimidinones and derivatives thereof, their synthesis and their use in treating sexual dysfunction in mammals, especially male erectile dysfunction. The phosphodiesterase V (PDEV) inhibitor, Sildenafil, 5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulphonyl)phenyl]-1-methyl-3-n-prpyl-6,7-dihydro-1H-pyazolo[4,3-d]pyrimidine-7-one, and a number of related analogues and their use are described in previous publications as well as in this patent. To date, at least nine families of mammalian PDEs have been described, five of which are capable of hydrolyzing the active, cGMP, to the inactive, GMP, under physiological conditions

(PDE's I, II, V, VI and IX). PDE V is the predominant isoform in human corpus cavernosum. Inhibitors of PDEV, therefore, would be expected to increase the concentration of cGMP in the corpus cavernosum and enhance the duration and frequency of penile erection (col. 1, lines 14-18, 60-66; col. 2, lines 37-51).

Sui also teaches the methods of treating sexual dysfunction, especially male erectile dysfunction, and/or impotence in a subject in need thereof comprising administering to the subject a therapeutically effective amount of any of the compounds or pharmaceutical compositions described. Also a process for making a pharmaceutical composition comprising any of the compounds and a pharmaceutically acceptable carrier (col. 5, lines 49-63).

Sui discloses that some of the compounds may form solvates with water (i.e, hydrates) or common organic solvents (col. 7, lines 55-59).

Sui discloses pharmaceutical compositions comprising one or more compounds of this invention in association with a pharmaceutically acceptable carrier. The **preferred** dosage forms are such as tablets, pills, capsules, powders, granules, parenteral solutions and suspensions, metered aerosol or liquid sprays, drops, ampules, autoinjector devices or administration by inhalation or insuffation (col. 9, lines 55-65).

Sui discloses the other derivatives and forms of the inhibitor of cGMP PDE and the method of making compositions in columns 14-30.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made, given the preferred agents and compositions for treating erectile

dysfunction of WO 9428902, to have looked in the art for preferred routes of administration for such agents as taught by Sui et al with the reasonable expectations of treating the patients with the most appropriate and convenient dosage form. The advantages of administration by inhalation are well known by those with ordinary skill in the art, which include immediate release, by-passing digestive system and avoiding pain and discomfort of injections.

Claims 25, 28 and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 9428902 in view of Sui et al (6,077,841) as applied to claims 21, 26, 27, and 29-31 above and further in view of Purewal et al (5,225,183).

The combined references, discussed above, lack specific teachings on the use of propellants.

Purewal teaches medicinal aerosol formulations. The suitable propellants are such as 1,1,1,2-tetrafluoroethane, n-butane, isobutane, pentane and isopentanes (col. 1, lines 58-66; col. 2, lines 14-30).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made given the general teachings of compositions of the combined references for treating sexual dysfunction through administration by inhalation of an inhibitor of cGMP PDE to a subject in need of such treatment, to have looked in the art

for more specific parameters such as propellants because of the expectations of successfully preparing an effective aerosol or spray form of the said inhibitor.

Response to Arguments

Applicant's arguments with respect to claims 21-29 have been considered but are moot in view of the new ground(s) of rejection. However the arguments regarding Sui et al reference will be addressed since this reference is maintained as a prior art in the new rejection.

Applicant argues that Sui describes shortcomings of utilizing the PDEV inhibitors, sildenafil and analogues, as an orally effective medication to treat ED, and discourages the use of sildenafil and its analogues in its orally administrable form let alone in inhalable form. This is not commensurate with the scope of the claims because the claims are to method of treating sexual dysfunction comprising administering by inhalation an effective amount of an inhibitor of cGMP PDE V....Sui discloses substituted 5-heterocyclyl pyrazolopyrimidinones useful for treatment of sexual dysfunction, which may be administered in the forms of powders, solutions or suspensions, by oral, parenteral, intranasal, inhalation, etc. The synthesis of compounds of the invention are disclosed. The disclosure of the side effects of sildenafil or its administration limitation to patients with underlying disorders do not negate the reference's teachings and disclosure on the method of treatment and the preferred routes of administration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mina Haghighatian
April 8, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER